INNER HEALTH

ANTIBIOTIC RESTORATION

RESTORE-BIOTIC

- ✓ Maintains good gut bacteria during antibiotics
- ✓ Helps restore healthy gut bacteria after antibiotics
- ✓ Supports a healthy immune response to break the cycle of sickness

FORMULATION DETAILS:

Each capsule contains:

Lactobacillus rhamnosus (LGG®)	20 Billion CFU
Bifidobacterium animalis ssp *lactis* (BB-12®)	10 Billion CFU
Lactobacillus acidophilus (LA-5™)	1 Billion CFU

LGG®, BB-12® & LA-5™ are registered trademarks of Chr. Hansen A/S

PATIENT INSIGHT

- Over 26 million antibiotic prescriptions are filled in Australia each year, with 50% of antibiotic users being dispensed a repeat prescription.[1]
- Microbiome disruption as a result of antibiotic use can last for up to four years and is commonly asymptomatic.[2]
- Gut health is intrinsically linked to immune and whole-body health, with an awareness of gut health increasing in the community.[3]
- A majority of the population is aware of antimicrobial resistance (AMR), and that without action, further spreading of antibiotic resistance throughout the community may result in resistances to frontline antibiotics.[4]

CLINICAL FOCUS:

- Maintaining and restoring the health of the microbiome during and after antibiotic use.[5,6,7]
- Those who wish to support their immune system to break the cycle of sickness.[8,9]
- Those who experience antibiotic associated diarrhoea (AAD) due to pathogenic organism overgrowth.[10]
- Community concern for antibiotic resistant bacteria spread through the microbiome due to dysbiosis.[11]

KEY FORMULA FEATURES:

- LGG® is the original, authenticated strain of the world's most researched probiotic.[12]
- BB-12®, the world's most researched bifidobacteria.[13]
- At a researched dose of 20 billion CFU/day, LGG® has been found to
  - Increase common native commensal bacteria.[14]
  - Assist in reducing antibiotic resistant organism spread during and following a course of antibiotic treatment.[5]
  - Maintain healthy immune responses.[8]
- Formulated to take alongside antibiotics.

KEY ACTIONS:

- LGG® enhances the colonisation of native gut bacteria to restore the microbiome for whole body health[14]
- LGG®, BB-12® & LA-5™ restore the species and health of the gut microbiome after antibiotic use[7,15]
- LGG® & BB-12® adhere to the gut wall in order to help repopulate the intestine and disrupt potential pathogen colonisation[13,16]
- LGG® interacts with immune cells in gut-associated lymphoid tissue (GALT) to influence and modulate immune responses[17]

PROFESSIONAL PRESCRIBING GUIDELINES:

Dosage & Directions

Adults and children over 5 years: Take 1 capsule daily during antibiotic course and for 14 days after to restore healthy gut bacteria balance and immunity. Take two hours apart from antibiotic dose.

Contraindications

None of note.

Cautions – Low level

Immunosuppressants: Theoretically, Lactobacillus could cause infection in patients taking medications that suppress the immune system. These include cyclosporine (Neoral, Sandimmune), tacrolimus (Prograf), azathioprine (Imuran), and cancer chemotherapeutic agents like cyclophosphamide (Cytoxan) and cisplatin (Platinol-AQ), and others.[18,19] Use only under medical supervision in these patients.

Severely ill and/or immunocompromised patients: Lactobacillus bacteraemia and sepsis have been reported in severely ill and/or immunocompromised patients consuming probiotics such as lactobacillus, though this is a very rare finding.[18,19] Based on these occurrences, a theoretical concern of bacteraemia and sepsis extends to bifidobacteria probiotics. [19,20] Use lactobacilli and bifidobacteria strains only under medical supervision in hospitalised patients.

Short-bowel syndrome: Patients with short-bowel syndrome might be predisposed to pathogenic infection from lactobacillus. This might be due to impaired gut integrity in patients with short-bowel syndrome. Use only under medical supervision in patients with this condition.[18,19]

Pregnancy:

Likely safe. While there is evidence to support the use of these ingredient during pregnancy[21,22,23,24,25] and a review did not identify concerns for use, Practitioner discretion is advised

Breastfeeding:

Appropriate for use.[21,22,23,26,27]

Children:

Appropriate for use.[8,19,28]

Prescribing tips and notes:

Antibiotics: Concomitant administration of antibiotics might decrease the effectiveness of lactobacilli and bifidobacteria. However, concomitant use of probiotics reduces the likelihood of gastrointestinal and genitourinary side effects and co-administration is considered beneficial. Separate administration of antibiotics and probiotics by at least two hours.[18,19]

No added: Artificial flavourings, colourings or preservatives.

Free from: Gluten, wheat, dairy, lactose, cereals, eggs, soy, nuts.

Suitable for vegans & vegetarians.

HCP COUNSELLING QUESTIONS

Can I take Inner Health Restore-Biotic if I am taking antibiotics?
Yes, Inner Health Restore-Biotic can be taken alongside antibiotics. Be sure to separate your dose of Inner Health Restore-Biotic, and your antibiotic dose, by at least two hours.

When should I start taking Inner Health Restore-Biotic?
Commence Inner Health Restore-Biotic on the first day of antibiotic treatment, and continue for the duration of your antibiotic course, and for 14 days following.

Can I take Inner Health Restore-Biotic if I am a vegan?
Yes, Inner Health Daily Restore-Biotic is formulated with plant-based ingredients and is suitable for use by vegans and vegetarians.

Is antibiotic resistance something I really need be concerned about?
Antibiotic resistance is a global health concern related to the use of antibiotics. If you take antibiotics, reducing the risk of resistance spread by using specific probiotic strains such as LGG® is advised.

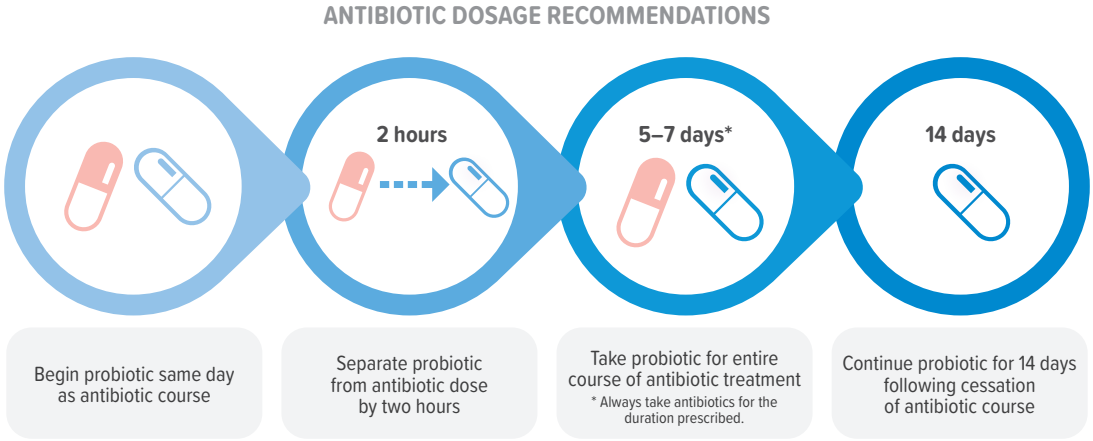
What is the best way to take Inner Health Restore-Biotic?
In order to ensure a two hour period between antibiotic doses and your daily dose of Inner Health Restore-Biotic, take your antibiotic first and wait two hours to take your probiotic e.g. when taking a once daily antibiotic, take this with your evening meal, and take Inner Health Restore-Biotic before you retire to bed.

I have previously recommended *Saccharomyces boulardii* (SB) for use alongside antibiotics. What makes Inner Health Restore-Biotic different to an SB formulation?
Inner Health probiotics use the Right Strain, at the Right Dose for the Right Condition. Whilst SB, which is best kept in the fridge for optimal stability, can assist the 5-15% of people affected by AAD,[29] and contribute to microbiome restoration, studies indicate that the most effective dosing regimen for SB use alongside antibiotics is several times a day.[30]
However, most people taking antibiotics won't suffer from AAD and instead, the researched strength and combination of LGG®, BB-12® and LA-5™ found in Inner Health Restore-Biotic will restore their microbiome and additionally support ongoing gut and immune health to help break the cycle of sickness with the added convenience of being one capsule a day as well as shelf stable.
For those customers who have previously experienced AAD, look to Inner Health Advanced with a combination of SB and LGG® that is taken twice a day and can be found in the fridge.

CLINICAL FEATURES

PATIENT DOSING REGIMEN

From first day of antibiotics take Inner Health Restore-Biotic once daily, and then also continue once daily for two weeks post antibiotic course. Take Inner Health Restore-Biotic 2 hours apart from antibiotic dose.



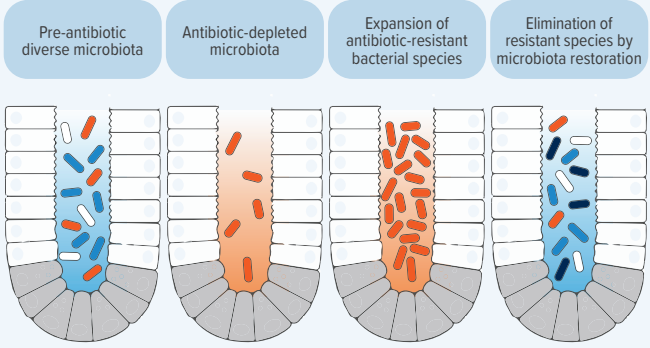
The human gut microbiome

The human gut microbiome consists of 37 trillion microorganisms, comprising of around 1000 species of bacteria. Whilst the composition of the gut microbiome varies between individuals, within population groups there is a general consistency within phyla and species, both beneficial and pathogenic.[31] This balance is influenced by a number of factors; diet, medication, age, feeding in infancy, all impact upon the diversity and abundance of the microbiome, with the goal of beneficial species impairing the overpopulation of disease-causing pathogenic species.[32]

Antibiotic impact upon the gut microbiome

Antibiotics contribute positively to a global reduction in morbidity and mortality against otherwise untreatable bacterial infections.[4] However, treatment with antibiotics is considered one of the most extreme perturbations to the human microbiome, comparable in impact with those that only happen shortly after birth or with inflammatory bowel conditions.[33] Additionally, these impacts can have systemic health implications, particularly on the immune system, such as recurrent illness,[34] decreases in vaccine efficacy,[35] and the development and overgrowth of antibiotic resistant strains.[11] Whilst for a small segment of the population, antibiotic use causes immediate gut dysfunction, as demonstrated by the occurrence of antibiotic-associated diarrhoea (AAD), the altered quantity and diversity of the microbiome can be impacted upon for much longer durations - for up to 4 years in fact.[2]

Antibiotic treatment eliminates many commensal bacteria species from the gut lumen and reduces antimicrobial defences



LGG®, BB-12® & LA-5™ for maintaining and restoring the health of the microbiome during and after antibiotic use

Pharmacists are in a unique position to recommend a specific probiotic to restore damage caused to the microbiome by antibiotics, not only to help reduce the spread of antibiotic resistance, but also for patients' whole-body health. However, not any probiotic will do. Different probiotic strains confer different benefits, at different doses, in different conditions, so it is important to recommend a probiotic with researched strains for microbiome health during and after antibiotic use. At a dose of 20 billion CFU/day, LGG® has been show to maintain the health and function of numerous key phyla in the healthy gut microbiome, including *Roseburia, Prevotella, Eubacterium, Coprococcus Ruminococcus* and *Blautia* genera (Figure 1)[6]. The mechanisms for this manipulation include the improvement of motility to allow GI mucosal penetration, and an increase in butyrate production by commensal bacteria, leading to an increase in fuel availability for these beneficial species.[14] LGG® and BB-12® also adhere to the gut wall during their transient gut population, enhancing their ability to support microbiome health.[13,16] These may also be the mechanisms behind LGG®'s ability to lower incidences of AAD and actively contribute to the restoration of a healthy microbiome.[5] Additionally, when used in combination with LGG®, probiotic strains BB-12® and LA-5™ have been found to maintain microbiome health whilst taking antibiotics as demonstrated by the 79% reduction in AAD in those consuming these strains (p=0.03).[15]

Genera directly enhanced by 20 billion LGG® after 28 days.[6]

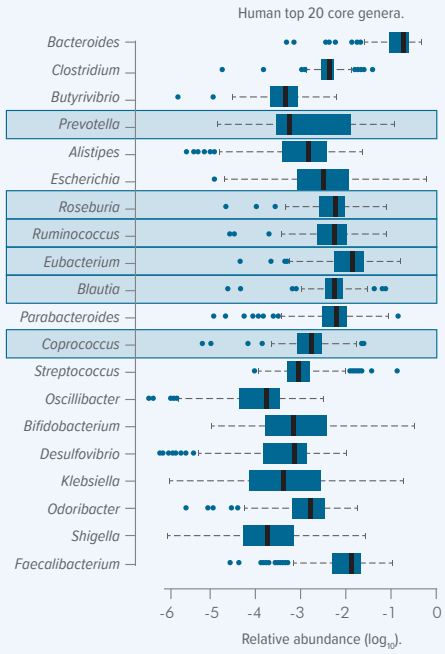


Figure 1 : Restoration of native commensal bacteria

LGG® can suppress antibiotic resistant pathogens

The most concerning aspect of antibiotic use is antibiotic resistance.[4] Rates of antibiotic resistance are increasing due to factors such as excessive use of some medications and the inappropriate prescribing of some antibiotics.[1]

LGG® has been shown in 2 hospital-run clinical trials to reduce the development of vancomycin resistant enterococci (VRE) in children[37] and adults.[38] In the adult trial, all patients in the LGG® treatment group were found to be VRE negative on study completion. Due to this success, control subjects who then crossed over into the treatment group were also all declared VRE negative after 4 weeks of LGG® treatment. Proposed mechanisms include competitively targeting colonisation sites of pathogenic bacteria, competing for fuel use, as well as through their direct antimicrobial and pH modification activities.[39]

LGG® and BB-12® Support Immune System Health in Adults and Children

Over 70% of the immune system resides in the gut. LGG® and BB-12® have been studied both alone and in combination with each other for their benefits to the immune system in both adult and child subjects.[13,41] Both probiotic strains have direct influence on immune cells in the GALT, reducing activation of various cytokines that would otherwise lead to inflammation. In one example of this, healthy college students, who are particularly susceptible to immune challenges due to their stress levels, received a supplement of LGG® and BB-12® or placebo. Those in the probiotic group had significantly shorter duration and severity of upper respiratory infection (URI) symptoms than their peers who received placebo (p=0.001), as well as significantly fewer missed school days (p=0.002).[9] LGG® showed similar results in decreasing risk of URI in children in a review encompassing over 1800 subjects.[42] LGG®[43] and BB-12®[44] also support gut barrier integrity, modulating immune responses to lower inflammation at the level of the individual enterocyte. This is important as bacterial translocation due to intestinal permeability can have systemic immune ramifications.[45] Additionally, LGG® has been found to increase mucosal IgA levels.[46]

References

1. Australian Commission on Safety and Quality in Health Care (ACSQHC). AURA. Sydney: ACSQHC; 2021 – Highlights. 14. Report No. 4
2. Jernberg C, Lofmark S, Edlund C, Jansson J. Long-term impacts of antibiotic exposure on the human intestinal microbiota. Microbiology. 2010; 15(Pt 11): p.3216-3223.
3. De Vos WM, Tilg H, Van Hul M, Cani PD. Gut microbiome and health: mechanistic insights. Gut. 2022; 71:1020-1032. doi:10.1136/gutjnl-2021-326789
4. World Health Organization (WHO). WHO Strategic Priorities on Antimicrobial Resistance: Geneva; 2022, 12.
5. Szajewska H, Kolodziei M. Systematic review with meta-analysis: Lactobacillus rhamnosus GG in the prevention of antibiotic-associated diarrhoea in children and adults. Aliment Pharmacol Ther. 2015;42(10):1149-57. doi: 10.1111/apt.13404.
6. Hauser G, Salkic N, Vukelic K, JajacKnez A, Stimac D. Probiotics for standard triple Helicobacter pylori eradication: a randomized, double-blind, placebo-controlled trial. Medicine (Baltimore). 2015;94(17): e685. doi:10.1097/MD.0000000000000685
7. de Vrese M, Kristen H, Rautenberg P, Laue C, Schrezenmeir J. Probiotic lactobacilli and bifidobacteria in a fermented milk product with added fruit preparation reduce antibiotic associated diarrhea and Helicobacter pylori activity. J Dairy Res. 2011 Nov;78(4):396-403. doi: 10.1017/S002202991100063X.
8. Floch MH, Kim AS. Barrier function and the immune response. In: Probiotics: a clinical guide. Minneapolis: Slack Incorporated. 2010:21-40.
9. Smith TJ, Rigassio-Radler D, Denmark R, Haley T, Touger-Decker R. Effect of Lactobacillus rhamnosus LGG® and Bifidobacterium animalis ssp. lactis BB-12® on health-related quality of life in college students affected by upper respiratory infections. Br J Nutr. 2013 Jun;109(11):1999-2007. doi:10.1017/S0007114512004138.
10. Agamennone V, Krul CAM, Rijkers G, Kort R. A practical guide for probiotics applied to the case of antibiotic-associated diarrhea in The Netherlands. BMC Gastroenterol. 2018 Aug 6;18(1):103. doi: 10.1186/s12876-018-0831-x.
11. Shaw L, Bassam H, Barnes C, Walker S, Klein N, et al. Modelling microbiome recovery after antibiotics using a stability landscape framework. The ISME Journal. 2019;(13): p. 1845-1856.
12. Valio R&D Mikko Ikonen. Scientific reference on Lactobacillus rhamnosus (LGG®) (ATCC-53103). 2014
13. Jungersen M, Wind A, Johansen E, Christensen JE, Stuer-Lauridsen B, Eskesen D. The Science behind the Probiotic Strain Bifidobacterium animalis subsp. lactis BB-12®. Microorganisms. 2014 Mar;2(2):92-110
14. Eloe-Fadrosh EA, Brady A, Crabtree J, Drabek EF, Ma B, Mahurkar A, et al. Functional Dynamics of the Gut Microbiome in Elderly People during Probiotic Consumption. Mbio. 2015;6(2):e00231-15. Available from doi: 10.1128/mbio.00231-15
15. Wenus C, Goll R, Loken EB, Biong AS, Halvorsen DS, Florholmen J. Prevention of antibiotic-associated diarrhoea by a fermented probiotic milk drink. Eur J Clin Nutr. 2008 Feb;62(2):299-301. Epub 2007 Mar 14. PubMed PMID: 17356555.
16. Apostolou E, Pelto L, Kirjavainen PV, Isolauri E. Differences in the gut bacterial flora of healthy and milk-hypersensitive adults, as measured by fluorescence in situ hybridization. FEMS Immunol Med Microbiol. 2001; 30(3): 217-221.
17. Zeuthen LH, Christensen HR, Frøkiaer H. Lactic acid bacteria inducing a weak interleukin-12 and tumor necrosis factor alpha response in human dendritic cells inhibit strongly stimulating lactic acid bacteria but act synergistically with gram-negative bacteria. Clin. Vaccine Immunol. 2006, 13(3):365.
18. Lactobacillus. In: Natural Medicines Comprehensive Database [database on the Internet]. Stockton (CA): Therapeutic Research Faculty; 1995-2018 [updated 2018 Mar 13; cited 2019 Jan 25]. Available from: https://naturalmedicines.therapeuticresearch.com/. Subscription required to view.
19. Braun L, Cohen M. Herbs and natural supplements: an evidence-based guide. 4th ed. Vol 2. Sydney (AU): Elsevier/Churchill Livingstone; 2015. p. 771-96.
20. Natural Medicines. Bifidobacteria. [Online]. 2015. Available from: https://naturalmedicines.therapeuticresearch.com/. [Cited 30/03/2017].
21. Elias J, Bozzo P, Einarson A. Are probiotics safe for use during pregnancy and lactation? Can Fam Physician. 2011 Mar;57(3):299-301.
22. Laitinen K, Poussa T, Isolauri E; Nutrition, Allergy, Mucosal Immunology and Intestinal Microbiota Group. Probiotics and dietary counselling contribute to glucose regulation during and after pregnancy: a randomised controlled trial. Br J Nutr. 2009 Jun;101(11):1679-87.
23. Luoto R, Laitinen K, Nermes M, Isolauri E. Impact of maternal probiotic-supplemented dietary counselling on pregnancy outcome and prenatal and postnatal growth: a double-blind, placebo-controlled study. Br J Nutr. 2010 Jun;103(12):1792-9.
24. Hajifaraji M, Jahanjou F, Abbasalizadeh F, Aghamohammadzadeh N, Abbasi MM, Dolatkhah N. Effect of probiotic supplements in women with gestational diabetes mellitus on inflammation and oxidative stress biomarkers: a randomized clinical trial. Asia Pac J Clin Nutr. 2018;27(3):581–91. doi:10.6133/apjcn.082017.03.
25. Dotterud CK, Avershina E, Sekelja M, et al. Does Maternal Perinatal Probiotic Supplementation Alter the Intestinal Microbiota of Mother and Child? J Pediatr Gastroenterol Nutr. 2015;61(2):200–207. doi:10.1097/MPG.0000000000000781.
26. Simpson MR, Avershina E, Storrø O, Johnsen R, Rudi K, Øien T. Breastfeeding-associated microbiota in human milk following supplementation with Lactobacillus rhamnosus GG, Lactobacillus acidophilus La-5, and Bifidobacterium animalis ssp. lactis Bb-12. J Dairy Sci. 2018;101(2):889–99. doi:10.3168/jds.2017-13411.
27. Fernández L, Langa S, Martín V, Jiménez E, Martín R, Rodríguez JM. The microbiota of human milk in healthy women. Cell Mol Biol (Noisy-le-grand). 2013 Nov 3;59(1):31-42.
28. Kalliomäki M, Salminen S, Poussa T, Arvilommi H, Isolauri E. Probiotics and prevention of atopic disease: 4-year follow-up of a randomised placebo-controlled trial. Lancet. 2003 May 31;361(9372):1869-71.
29. McFarland L. Antibiotic-associated diarrhea: epidemiology, trends and treatment. Future Medicine. 2008; 3(5): p. 563-578.
30. McFarland LV. Systematic review and meta-analysis of Saccharomyces boulardii in adult patients. World J Gastroenterol. 2010 May;16(18):2202-2222. doi:10.3748/wjg.v16.i18.2202
31. Binda C, Lopetuso LR, Rizzatti G, Gibiino G, Cennamo V, Gasbarrini A. Actinobacteria: a relevant minority for the maintenance of gut homeostasis. Dig Liver Dis. 2018 May;50(5):421-428. Available from doi: 10.1016/j.dld.2018.02.012.
32. Lynn DJ, Benson SC, Lynn MA, Pulendran B. Modulation of immune responses to vaccination by the microbiota: implications and potential mechanisms. Nat. Rev. Immunol. 2021 May. Available from https://doi.org/10.1038/s41577-021-00554-7
33. Bhalodi AA, van Engelen TS, Virk HS, Joost Wiersinga W. Impact of antimicrobial therapy on the gut microbiome. J Antimicrob Chemother. 2019; 74 Suppl 1: i6–i15. doi:10.1093/jac/dky530
34. de Koff EM, Man WH, van Houten MA, Vlieger AM, Chu ML, et al. Microbial and clinical factors are related to recurrence of symptoms after childhood lower respiratory tract infection. ERJ Open Research. 2021 Apr;7(2):0939-2020. doi: 10.1183/23120541.00939-2020

35. Hagan T, Cortese M, Rouphael N, Boudreau C, Linde C, Maddur MS, et al. Antibiotics-Driven Gut Microbiome Perturbation Alters Immunity to Vaccines in Humans. Cell. 2019 Sep 5;178(6):1313-1328.e13.

36. Pamer E. Resurrecting the intestinal microbiota to combat antibiotic-resistant pathogens. Science. 2016; 325(6285): p. doi:10.1126/science.aad9382.

37. Szachta P, Ignys I, Cichy W. An evaluation of the ability of the probiotic strain Lactobacillus rhamnosus GG to eliminate the gastrointestinal carrier state of vancomycin-resistant enterococci in colonized children. J Clin Gastroenterol. 2011; 45(10): p. 872-7.

38. Manley K, Fraenkel M, Mayall B, Power D. Probiotic treatment of vancomycin-resistant enterococci: a randomised controlled trial. Med J Aust. 2007 May; 186(9): p. 454-7.

39. McFarland L. Use of probiotics to correct dysbiosis of normal microbiota following disease or disruptive events: a systematic review. BMJ Open. 2014; 4.

40. Gill HS. Probiotics to enhance anti-infective defences in the gastrointestinal tract. Best Pract Res Clin Gastroenterol. 2003; 17(5):755-73. doi.org/10.1016/S1521-6918(03)00074-X

41. Capurso L. Thirty Years of Lactobacillus rhamnosus GG: A Review. J Clin Gastroenterol. 2019 Mar;53 Suppl 1: S1-S41. doi: 10.1097/MCG.0000000000001170."

42. Liu S, Hu P, Du X, Zhou T, Pei X. Lactobacillus rhamnosus GG supplementation for preventing respiratory infections in children: a meta-analysis of randomized, placebo-controlled trials. Indian Pediatr. 2013 Apr;50(4):377-81. "

43. Francavilla R, Miniello V, Magistà AM, De Canio A, Bucci N, Gagliardi F et al. A randomized controlled trial of Lactobacillus GG in children with functional abdominal pain. Pediatrics. 2010 Dec;126(6): e1445-52

44. Commane DM, Shortt CT, Silvi S, Cresci A, Hughes RM, Rowland IR. Effects of fermentation products of pro- and prebiotics on trans-epithelial electrical resistance in an in vitro model of the colon. Nutr Cancer. 2005;51(1):102-9.

45. Fasano A, Shea-Donohue T. Mechanisms of disease: the role of intestinal barrier function in the pathogenesis of gastrointestinal autoimmune diseases. Gastroenterol Hepatol (N Y). 2005;2(9):416-422

46. Piirainen L, Haahtela S, Helin T, Korpela R, Haahtela T, Vaarala O. Effect of Lactobacillus rhamnosus GG on rBet v1 and rMal d1 specific IgA in the saliva of patients with birch pollen allergy. Ann Allergy Asthma Immunol. 2008 Apr;100(4):338-42

RTN1793 - 06/22

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